PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

# Pegylated Liposomal Doxorubicin (Caelyx®) AIDS Related Kaposi's Sarcoma

**PROTOCOL REF: MPHACAESA**
**Version No: 1.0**

## Approved for use in:

- For treatment of advanced, symptomatic or rapidly progressive AIDS -related Kaposi's sarcoma (KS)
- Licensed in patients with low CD4 counts (< 200 CD4 lymphocytes/$mm^3$) and extensive mucocutaneous or visceral disease.
- Pegylated liposomal doxorubicin is considered standard of care first-line systemic chemotherapy for the treatment of AIDS-KS
- Treatment should be requested by a member of the infectious diseases team that specialises in HIV AIDs based at RLUH (see appendix 1).
- Pegylated liposomal doxorubicin **must not** be used to treat AIDS-KS that may be treated effectively with local therapy or systemic alfa-interferon.

## Dosage:

| Drug | Dose | Route | Frequency |
|---|---|---|---|
| **Pegylated liposomal doxorubicin (Caelyx®)** | **20mg/$m^2$** | IV infusion | Day 1 only of a 21 day cycle |

Pegylated liposomal doxorubicin should be continued for either 6 or 10 cycles as instructed by the Infectious Diseases team.

## Administration:

- Pegylated liposomal doxorubicin is not suitable for anyone with a peanut or soya allergy
- There is a lifetime cumulative anthracycline dose of 450 mg/m$^2$. Any doses above this dose require an echo prior to each dose.
- **Pregnancy and Breast-feeding**
    - Doxorubicin hydrochloride is suspected to cause serious birth defects when administered during pregnancy. Women of child-bearing potential must be advised to avoid pregnancy while they or their male partner are receiving Caelyx and in the six months following discontinuation of treatment.
    - Breastfeeding is contraindicated in those receiving Caelyx. Furthermore, breastfeeding is not recommended in HIV positive mothers due to the risk of HIV transition.

## Anti-emetic risk:

Mildly emetogenic.

## Supportive treatments:

Domperidone 10mg tablets, to be taken orally three times a day when required

## Extravasation risk:

Pegylated liposomal doxorubicin: IRRITANT

Refer to the CCC policy for the '[Prevention and Management of Extravasation Injuries]'.

## Interactions:

No formal medicinal product interaction studies have been performed with pegylated liposomal doxorubicin but care is required in the concomitant use of medicinal products known to interact with standard doxorubicin:-

- Doxorubicin undergoes metabolism via CYP450 so concomitant use of inhibitors may increase toxicity and inducers may reduce efficacy.
- Ciclosporin and cimetidine increase the AUC of doxorubicin; dose adjustments may be required.
- Barbiturates may lead to an accelerated plasma clearance of doxorubicin, while the concomitant administration of phenytoin may result in lower plasma phenytoin levels.
- Doxorubicin is a potent, radio-sensitizing agent.

## Treatment schedule:

| Day | Drug | Dose | Route | Diluent and rate |
|---|---|---|---|---|
| 1 | **Dexamethasone** | **8mg** | **PO** | 30 minutes before chemotherapy |
| | **Pegylated liposomal doxorubicin (Caelyx®)** | **20mg/m$^2$** | **IV** | In 250mls 5% glucose over 30 minutes. |

Every 21 days for 6 to 10 cycles

**In those patients who experience an infusion reaction**, the method of infusion should be modified as follows:

1. 5% of the total dose should be infused slowly over the first 15 minutes.
2. If tolerated without reaction, the infusion rate may then be doubled for the next 15 minutes.
3. If tolerated, the infusion may then be completed over the next hour for a total infusion time of 90 minutes.

Please refer to the **CCC Hypersensitivity; Management Prevention Policy**

## Main toxicities:

Thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea, infusion related reactions, cardiac toxicity, palmer-plantar erythrodysesthesia, mucositis, stomatitis.

## Investigations and treatment plan:

| | Pre | Cycle 1 | Cycle 2 | Prior to cycle 3 | Cycle 3 | Ongoing |
|---|---|---|---|---|---|---|
| Informed Consent | X | | | | | |
| Clinical Assessment | X | | | | X | As clinically indicated or at the end of treatment |
| OTR/ Go-ahead | X | | X | | X | Every cycle |
| SACT Assessment (to include PS and toxicities) | | X | X | | X | Every cycle |
| FBC | X | X | X | | X | Every cycle |
| U&E & LFTs & Magnesium | X | X | X | | X | Every Cycle |
| CrCl (Cockcroft and Gault) | X | X | X | | X | Every cycle |
| CT scan** | X | | | | | At the end of treatment and if clinically indicated |
| Echo/MUGA/ECG | | | | | | When clinically indicated based on cardiac risk factors an co-morbidities |
| ECG | | | | | | If clinically indicated |
| Blood pressure measurement | X | | | | | Repeat if clinically indicated |
| Respiratory Rate | | | | | | If clinically indicated |
| Weight recorded | X | X | X | | X | Every cycle |
| Blood glucose | X | | | | | Repeat if clinically indicated |

During treatment and for 6 months after, appropriate measures must be taken to avoid pregnancy; this applies to patients of both sexes

## Dose Modifications and Toxicity Management:

**Haematological toxicity:**

| ANC (x $10^9$/L) | Platelets (x $10^9$/L) | Action |
|---|---|---|
| ≥ 1.0 | ≥ 50 | Proceed with treatment |
| 0.5 to 0.9 | 25 to 49 | Wait until ANC ≥ 1.0 x $10^9$/L and/or platelets ≥ 50 x $10^9$/L and then restart at previous dose |
| <0.5 | <25 | Wait until ANC ≥ 1.0 x $10^9$/L and/or platelets ≥ 50 x $10^9$/L and then decrease dose by 25% or continue previous dose with GCSF support |

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

## Dosing in renal and hepatic impairment:

| **Hepatic impairment** | |
|---|---|
| **Bilirubin (micromole/L)** | **Dose adjustment** |
| 20 to 50 | 75% of original dose for the first cycle. If tolerated without an increase in bilirubin or ALT then dose can be increased to 100% for cycle 2 |
| >51 | 50% of original dose for the first cycle. If tolerated without an increase in bilirubin or ALT then dose can be increased to 75% for cycle 2 and 100% for cycle 3. |

| **Renal impairment** | |
|---|---|
| **CrCl (ml/min)** | **Dose** |
| ≥ 30 | 100% |
| < 30 | Not studied. No dose adjustments expected. |

## References:

1. Caelyx pegylated liposomal 2 mg/ml concentrate for solution for infusion, summary of Product Characteristics, Baxter Healthcare Limited available via https://www.medicines.org.uk/emc (last updated 27th September 2021).
2. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08.
3. British HIV Association guidelines for HIV-associated malignancies 2014

## Appendices

## Appendix A

Prescribing will be delivered by the Clatterbridge Sarcoma Team. Contact details for the infectious diseases for patient specific clinical queries are enclosed below.

| Prescriber | Role | Contact details |
|---|---|---|
| Eimear Kealey | HIV specialist nurse | 0151 706 2966<br>Eimear.Kealey@liverpoolft.nhs.uk |
| Anne Neary | ID pharmacist | via RLUH switch Bleep 4502<br>Anne.Neary@liverpoolft.nhs.uk |
| Dr Libuse Ratcliffe | ID Consultant | Secretaries – via RLUH switch<br>Libuse.Ratcliffe@liverpoolft.nhs.uk |
| Dr Nicholas Wong | ID Consultant | Secretaries – via RLUH switch<br>Nicholas.Wong@liverpoolft.nhs.uk |

## Circulation/Dissemination

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|---|---|
| Date added into Q-Pulse | 22nd November 2021 |
| Date document posted on the Intranet | 22nd November 2021 |

## Version History

| Date | Version | Author name and designation | Summary of main changes |
|---|---|---|---|
| October2021 | 1.0 | Rob Challoner - Lead Pharmacist for Inpatient Care | New protocol |
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